

## **REMARKS**

### **I.     Status of the Claims**

Claims 1-101 were filed with the application. Claims 1-58, 60, 63-69 and 71-101 have been canceled. Thus, claims 59, 61, 62 and 70 are under consideration and have been examined. Claims 59, 61, 62 and 70 are again presented for reconsideration. All claims are rejected under 35 U.S.C. §112, second paragraph, and 35 U.S.C. §103. Claims 59, 62 and 70 stand rejected under 35 U.S.C. §102. The specific grounds for the §102 rejection, and applicants' response thereto, are set out in detail below. Applicants hereby concurrently file a notice of appeal to the §112 and §103 rejections and reiterate their previous response to these rejections as stated below.

### **II.    Rejections Under 35 U.S.C. §102(e)**

Claims 59, 62 and 70 stand rejected under 35 U.S.C. §102(e) for allegedly being anticipated by U.S. Patent 6,673,604. In response applicants submit a Declaration under 37 C.F.R. §1.131 and new supporting documentation. This Declaration coupled with the supporting documentation provided with the Declaration previously on record (submitted February 24, 2004), establishes conception and reduction to practice prior to this reference, and demonstrates diligence up to the date of filing, thereby removing the reference as available prior art for a §102(e) rejection. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

### **III.   Rejections Under 35 U.S.C. §112, Second Paragraph**

The examiner has repeatedly rejected claims 59, 61, 62 and 70 under the second paragraph of §112 as being indefinite for failing to particularly point out and distinctly claim the

subject matter. Applicants contend the argument presented in both the Response filed on January 31, 2005 and the Appeal Brief previously on record should be sufficient to overcome all §112 objections to the claims as currently written. That argument, restated here for clarity, is that the very essence of the present claims is to identify molecules that may modify MCIP expression *in either direction – up or down*; hence the use of the word *modulation*, which is generic to up- or down-regulation, accurately reflects the intent of the claim, and is thus very much correct in its usage. By way of example, the Merriam-Webster dictionary defines modulate as to “vary” or “adjust” or “alter” and does not describe a direction in which such variation or adjustment occurs. A modulator is thus, by definition, something that is capable of varying something else, and a modulator of MCIP expression can therefore vary the expression of MCIP in any direction, up or down. There is nothing indefinite about this recitation, and reversal of this rejection is respectfully requested.

In the most recent Office Action, the examiner again objects to claims 61 and 62 by arguing that a modulator cannot be both an agonist and an antagonist, and hence alleges these recitations in claims 61 and 62, respectfully, are also unclear. Nothing could be further from the truth. Claims 61 and 62 are dependent claims. Thus, they further limit the subject matter of claim 59, which as already pointed out, is generic with respect to the direction of regulation. There is absolutely nothing indefinite about these claims, and in point of fact these claims address the issue raised by the examiner’s faulty rejection of the word modulator by giving a specific direction to the modulation that must occur. Reversal of this rejection is respectfully requested as well.

Claim 70 is also rejected over the term “second pharmaceutical agent.” Applicants previously amended claim 70 to clarify that the second pharmaceutical agent is distinct from the agent provided in claim 59. Applicants have previously attempted to amend claim 59 to specify a first pharmaceutical agent (*i.e.*, the modulator), in that claim, but entry of this amendment was denied. Applicants are more than willing to provide an additional amendment, or authorize the examiner to make such an amendment. Even if this amendment is not entered, however, appellants submit that one of skill in the art would recognize that the “second pharmaceutical agent” of claim 70 is in addition to the modulator of claim 59, and thus there is no issue of indefiniteness. Reversal of this rejection is respectfully requested.

#### **IV. Rejections Under 35 U.S.C. §103**

Claims 59, 61, 62 and 70 are rejected under 35 U.S.C. §103(a) as allegedly being obvious in light of Chin *et al.*, and Sussman *et al.* The examiner alleges that these references, which teach the inhibition of calcineurin with calcineurin inhibitors, make obvious the claims of modulating MCIP, since MCIP was later found to be both activated by and capable of modulating the activity of calcineurin. Applicants again contend, as stated in the prior response, that in order to make modulation of MCIP obvious in light of these references, the examiner is improperly relying on inherency in the context of an obviousness rejection, since MCIP’s relation to calcineurin was not even known at the time these references published. The proper analysis of references that are used to support an obviousness rejection should focus on whether the references would render the invention obvious based on the knowledge that one of skill in the art would gain from the references, not based on what is later discovered to be true. The fact that a specific result or pathway might flow inherently from the practice of a process or

discovery of a partial biological pathway is immaterial if the skilled artisan “would not appreciate or recognize that inherent result.” *In re Naylor*, 152 USPQ 106 (CCPA 1966). Furthermore, *In re Spormann*, 150 USPQ 449 (CCPA 1966) says that “the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.” That statement describes the current situation since both of the cited references existed before the knowledge of MCIP’s role in cardiac biology was fully elucidated. The fact that it was later discovered that calcineurin could modulate MCIP would not and could not make it obvious to one of skill in the art, prior to that discovery, that modulating MCIP could be accomplished by modulating calcineurin. In other words, since MCIP’s relationship to calcineurin was “unknown” at the time these references published, they cannot be used as “predicates” for an obviousness rejection.

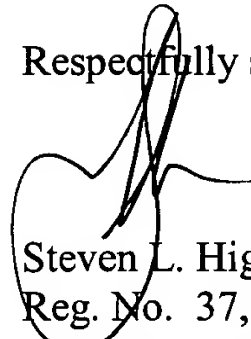
Perhaps even more to the point, neither reference renders obvious the steps of (i) selecting a human patient or (ii) selecting a modulator of MCIP with which to treat that human patient, both of which are affirmative recitations in the instant claims, for the simple reason that *neither step is taught or suggested by the references*. Thus, the examiner has simply ignored required elements of the claims, relying instead on the flawed inherency argument to support an obviousness rejection. As stated above, this is not proper. In light of these statements, reconsideration and reversal of these rejections is respectfully requested.

#### IV. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to this effect is earnestly solicited. Should Examiner Liu have any questions regarding this response, he is invited to contact the undersigned attorney at

(512) 536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Steven L. Highlander", is written over the typed name and registration number.

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